General

Guideline Title

Antithrombotics: indications and management. A national clinical guideline.

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Antithrombotics: indications and management. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Jun. 68 p. (SIGN publication; no. 129). [238 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Antithrombotic therapy. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 1999. 70 p. (SIGN publication; no. 36). [186 references]

Any updates to the guideline that result from the availability of new evidence will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site.

This guideline was republished in June 2013.

Recommendations

Major Recommendations

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the full-text guideline document.

Note from SIGN: Following the approval in February 2013 of apixaban by the Scottish Medicines Consortium (SMC) for prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, a recommendation was added to the "Novel Antithrombotics in AF" section to reflect this new treatment option.

The grades of recommendations (A-D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Antiplatelet Agents

A - To minimise the risk of bleeding, the lowest recommended dose of aspirin should be used for the clinical indication.

Parenteral Anticoagulation

Unfractionated Heparin

Initiation, Dosage and Monitoring

B - In patients given treatment dose unfractionated heparin therapy, routine monitoring of the activated partial thromboplastin time (APTT) ratio (at least daily) and adjustment of heparin doses according to a local protocol, to achieve the target therapeutic range of anticoagulant effect (APTT ratio) is recommended.

Low Molecular Weight Heparins (LMWH)

Monitoring

D - LMWH should be used with caution for those in whom standard or weight-adjusted dosing is likely to be unreliable, especially in:

- Patients with acute kidney injury or stage 4-5 chronic kidney disease
- Patients in extreme weight ranges
- Pregnant women
- Neonates and infants

Oral Anticoagulation with Vitamin K Antagonists (VKA)

Management of VKA Therapy for Invasive Procedures

A - Vitamin K antagonists should not be discontinued in patients undergoing outpatient dental surgery, including dental extraction.

D - Decisions regarding interruption of VKA therapy for other surgical and invasive procedures, and whether bridging therapy is advisable, should be made on an individual basis dependent upon the perceived risks of bleeding and thrombosis associated with continuation of anticoagulation and discontinuation of anticoagulation, respectively, and the nature of the proposed procedure.

Recommencing VKA Therapy After a Major Bleeding Event

C - Patients with a mechanical prosthetic heart valve who suffer intracranial haemorrhage should, following a careful risk/benefit analysis, be considered for reintroduction of long term VKA therapy after 7-14 days, possibly at a reduced target international normalised ratio (INR).

C - Patients who suffer gastrointestinal haemorrhage and who require to start or continue a VKA should be considered for delayed initiation or temporary cessation of therapeutic anticoagulation for 21 days or until there is evidence of healing of the bleeding lesion.

Pharmacogenomics and Warfarin

A - Pharmacogenetic testing prior to initiation of therapy with a vitamin K antagonist is not recommended.

Atrial Fibrillation (AF): Prophylaxis of Systemic Embolism

Efficacy of Warfarin and Aspirin as Antithrombotic Prophylaxis

Monotherapy

D - In all patients with AF, risk factors for systemic thromboembolism should be assessed routinely using $CHADS_2$ or CHA_2DS_2-VASc score.

B - Patients with AF who are clearly low risk, (age<65 and lone AF) do not require antithrombotic therapy. This applies to male patients with CHA_2DS_2-VASc score=0 and female patients with CHA_2DS_2-VASc score=1 in whom the single point is allocated due to female sex.

A - All patients with AF who have a $CHADS_2$ or CHA_2DS_2-VASc score of ≥1 (one or more clinically relevant risk factors) should be considered for warfarin at a target INR of 2.5 (range 2.0-3.0) or a newer anticoagulant. The balance of risks and benefits of anticoagulant therapy should be assessed and discussed annually with the patient, with consideration given to patient preference.

A - Antiplatelet therapy should only be considered where warfarin or one of the alternative new anticoagulants has been declined.

Combination Therapy with Aspirin and Warfarin

A - In patients with AF the combination of aspirin and warfarin is not recommended.

A - If warfarin is indicated for moderate-or high-risk AF it should be used alone even in the presence of concomitant stable cardiovascular

disease.

Cardioversion

D - Cardioversion of AF should be considered in selected patients.

D - Patients with very recent onset AF (48 hours or less) being considered for urgent cardioversion require immediate assessment and treatment with heparin.

D - If it is certain that AF has been present for two days or less, cardioversion may be attempted electrically or pharmacologically without prior oral anticoagulation.

D - If AF has been present for more than two days, warfarin should be given to reduce the risk of thromboembolism for three weeks before cardioversion and continued for at least four weeks after cardioversion.

Novel Antithrombotics in AF

Dabigatran Etexilate

A - Dabigatran etexilate can be considered as an alternative to warfarin in the management of patients with atrial fibrillation with one or more risk factors for stroke.

Rivaroxaban

A - Rivaroxaban can be considered as an alternative to warfarin in the management of patients with atrial fibrillation with one or more risk factors for stroke.

Apixaban

A - Apixaban can be considered as an alternative to warfarin in the management of patients with atrial fibrillation with one or more risk factors for stroke.

Other Cardiac Causes of Systemic Embolism

Rheumatic Mitral Valve Disease

D - Long term warfarin prophylaxis (target INR 2.5, range 2.0-3.0) should be considered in patients with rheumatic mitral valve disease and recommended if the patient is in atrial fibrillation.

Mitral Valve Prolapse, Mitral Annular Calcification and Isolated Aortic Valve Disease

D - Long term warfarin prophylaxis (target INR 2.5, range 2.0-3.0) is recommended for patients with mitral valve prolapse, mitral annular calcification, or isolated aortic valve disease only in the presence of previous systemic embolism or atrial fibrillation.

Mechanical Heart Valves

D - Patients with mechanical heart valves should receive long term prophylaxis with warfarin.

D - The target INR should depend upon type and position of valve (aortic or mitral) and cardiac factors specific to the patient.

A - Addition of aspirin or dipyridamole should be considered in patients with mechanical heart valves who suffer systemic embolism despite adequate intensity warfarin.

Acute, Obstructive Heart Valve Thrombosis

D - Systemic thrombolysis is recommended for the initial treatment of acute obstructive prosthetic heart valve thrombosis.

Bioprosthetic Heart Valves

D - Low-dose aspirin (75 mg daily) is recommended in patients with a bioprosthetic valve in the aortic position who have no other indication for VKA therapy.

D - Patients with a bioprosthetic valve in the mitral position should receive three months treatment with warfarin (target INR 2.5) followed by low-dose aspirin if in sinus rhythm and with no indication to continue warfarin.

D - Patients with a bioprosthetic valve and a history of systemic embolism should receive at least three months of anticoagulation after valve insertion with warfarin, target INR of 2.5.

D - Patients with a bioprosthetic valve and left atrial thrombus at surgery should receive warfarin (target INR 2.5) until the clot has resolved.

D - Patients with a bioprosthetic valve and other risk factors such as atrial fibrillation and low ventricular ejection fraction should receive long term warfarin (target INR 2.5).

B - Selected patients with prosthetic valves may receive aspirin as additional therapy.

Primary Prophylaxis of Vascular Disease

Aspirin

A - Aspirin is not recommended for primary prevention of vascular disease when benefits are considered against the increased risk of hemorrhage.

Peripheral Arterial Disease (PAD)

Antiplatelet Agents

Percutaneous Transluminal Angioplasty in the Lower Limbs

A - Antiplatelet therapy is recommended for patients with symptomatic peripheral arterial disease.

Oral Anticoagulation

A - In patients with PAD who have an indication for treatment with a vitamin K antagonist aspirin should not be added to improve anticoagulation.

Parenteral Anticoagulation

Intermittent Claudication

B - Heparin is not indicated in the management of intermittent claudication.

Bypass Surgery for Lower Limb Ischaemia

B - Further treatment with LMWH after bypass surgery is not recommended.

Thrombolytic Therapy

Acute Peripheral Arterial Occlusion

B - In individual patients with acute peripheral arterial occlusion catheter-directed intra-arterial (CDIA) is preferred to systemic thrombolysis. In assessing the individual patient the increased risk of haemorrhagic adverse events (including stroke) associated with CDIA thrombolytic therapy should be balanced against the risks of anaesthesia and surgery.

Cerebrovascular Disease

Acute Prophylaxis of Further Vascular Events

Antiplatelet Agents

A - Aspirin 300 mg should be commenced within 48 hours of ischaemic stroke and continued for at least 14 days.

Parenteral Anticoagulation

A - The routine use of anticoagulants is not recommended for the treatment of acute ischaemic stroke.

A - Anticoagulants are not recommended in patients with progressing stroke.

A - In patients at high risk of venous thromboembolic disease LMWH should be considered in preference to unfractionated heparin (UFH).

D - Following administration of intravenous thrombolysis, heparin should not be given in any form for 24 hours.

C - Intravenous UFH or subcutaneous LMWH followed by warfarin therapy should be considered in patients with cerebral venous thrombosis.

Acute Stroke and Atrial Fibrillation

D - In patients with AF and acute stroke:

- In the absence of haemorrhage, anticoagulant therapy should begin after two weeks but may be delayed in the presence of a large infarct.
- In the presence of haemorrhage, anticoagulant therapy should not be given.

Parenteral Thrombolytic Therapy

A - Patients admitted with stroke within four and a half hours of definite onset of symptoms, who are considered suitable, should be treated with 0.9 mg/kg (up to maximum 90 mg) intravenous recombinant tissue plasminogen activator (rt-PA).

A - Onset to treatment time should be minimised.

A - Systems should be optimised to allow the earliest possible delivery of intravenous rt-PA within the defined time window.

A - Streptokinase should not be used for treatment of patients in the acute phase of stroke.

Secondary Prevention After Acute Ischaemic Stroke or Transient Cerebral Attack

Antiplatelet Therapy

A - Clopidogrel monotherapy (75 mg daily) or aspirin (75 mg) in combination with dipyridamole (200 mg extended release twice daily) should be prescribed after ischaemic stroke or transient ischaemic attack for secondary prevention of vascular events.

Carotid Endarterectomy (CEA)

A - Standard antiplatelet treatment should be given after CEA.

<u>Myeloproliferative Disorders</u>

B - Patients with polycythaemia rubra vera should be considered for treatment with aspirin, unless there are contraindications.

<u>Intravascular Devices</u>

Prevention of Deep Vein Thrombosis (DVT) due to Central Venous Catheters

C - The risk/benefit ratio of the use of thromboprophylaxis in patients with central venous catheters should be considered on an individual basis.

C - Thromboprophylaxis in patients with central venous catheters is not routinely recommended.

Patients with Cancer

A - Neither warfarin nor heparin should be used routinely to prevent catheter-related deep vein thrombosis in cancer patients.

Maintaining Patency of Arterial and Venous Catheters

Parenteral Anticoagulation

B - Normal saline should be used to maintain the patency of arterial catheters.

Thrombolytic Therapy

B - For occluded non-haemodialysis central venous catheters local treatment with short dwell instillation of thrombolytic agent is recommended.

<u>Pregnancy</u>

Pregnancy Failure

Women with Acquired Thrombophilia

B - Prophylactic doses of heparin with or without low-dose aspirin may be considered in women with antiphospholipid antibodies and recurrent pregnancy failure or fetal death in whom no other cause is identified.

Women with Recurrent Miscarriage and no Known Thrombophilia

A - Antithrombotic therapy is not indicated in the management of recurrent miscarriage in the absence of antiphospholipid syndrome.

Mechanical Heart Valves

C - In women with mechanical prosthetic heart valves the treatment options are:

- Adjusted-dose, 12 hourly, subcutaneous LMWH throughout pregnancy with anti-Xa monitoring
- Adjusted-dose, 12 hourly, subcutaneous UFH throughout pregnancy with APTT monitoring or anti-Xa monitoring
- Adjusted-dose UFH or LMWH from ≤6 to 13 weeks gestation, followed by warfarin until two weeks before delivery when heparin is reintroduced.

Models of Care

A - Self monitoring and self dosing is safe and effective and can be considered for some patients.

B - Computer-assisted dosing should be considered.

Definitions:

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Atrial fibrillation
- Peripheral arterial disease
- Cerebrovascular disease
- Pregnancy
- Patients with intravascular devices

Note: The use of antithrombotic therapy in the management of established ischaemic heart disease is not included, but is covered in SIGN's suite of cardiovascular guidelines.

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Cardiology

Dentistry

Family Practice

Nursing

Obstetrics and Gynecology

Pharmacology

Pulmonary Medicine

Surgery

Intended Users

Advanced Practice Nurses

Dentists

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To provide recommendations based on current evidence for best practice in the management of adult patients on antithrombotic therapy

Target Population

Adult patients on antithrombotic therapy

Interventions and Practices Considered

1. Antiplatelet agents: aspirin, dipyridamole, clopidogrel
2. Parenteral anticoagulation: unfractionated heparin (UFH) and low molecular weight heparin (LMWH), fondaparinux, danaparoid
3. Oral anticoagulation with vitamin K antagonists (VKA): warfarin
4. Novel antithrombotic agents
5. Combination therapy
6. Assessment of risk factors using $CHADS_2$ or CHA_2DS_2-VASc
7. Special considerations:
    - Atrial fibrillation (AF): prophylaxis of systemic embolism
    - Systemic embolism in other cardiac conditions
    - Primary prophylaxis of vascular disease
    - Peripheral arterial disease
    - Cerebrovascular disease
    - Myeloproliferative disorders
    - Intravascular devices
    - Pregnancy
8. Patient education on self-monitoring and computer-assisted dosing

Major Outcomes Considered

- Positive and negative predictive value of diagnostic tests
- Risk factor score ($CHADS_2$ or CHA_2DS_2-VASc)
- Rate of major bleeding episodes, including intracranial bleeding
- Risk of myocardial infarction, stroke, systemic embolism, and other cardiovascular events
- Adverse effects of antithrombotic therapy
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review

The evidence base for this guideline was synthesised in accordance with Scottish Intercollegiate Guidelines Network (SIGN) methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Databases searched include Medline, Embase, Cinahl, PsycINFO and the Cochrane Library. The year range covered was 2003-2009. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

Literature Search for Patient Issues

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to early management of patients with a head injury. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised and presented to the guideline development group.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

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2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result

of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgment. The extent to which a study meets a particular criterion (e.g., an acceptable level of loss to follow up) and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN Executive staff will arbitrate to reach an agreed quality assessment.

Evidence Tables

Evidence tables are compiled by SIGN executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]). Available from the SIGN Web site .

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Synthesising the Evidence

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgment is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgment on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable.

It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

Considered Judgment

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of considered judgment.

Under the heading of considered judgement, guideline development groups summarise their view of the total body of evidence covered by each evidence table. Each guideline group considers the following factors:

- Quantity, quality, and consistency of evidence
- External validity (generalisability) of studies.
- Directness of application to the target population for the guideline.
- Any evidence of potential harms associated with implementation of a recommendation.

- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them in accordance with the recommendation)
- Whether, and to what extent, any equality groups may be particularly advantaged or disadvantaged by the recommendations made.
- Implementability (i.e., how practical it would be for the National Health Service (NHS) Scotland to implement the recommendation).

Then the group is asked to summarise its view on all of these issues, both the quality of the evidence and its potential impact, before making a graded recommendation. This summary should be succinct, and taken together with its views of the level of evidence represent the first draft of the text that will appear in the guideline immediately before a graded recommendation.

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN Web site .

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development.

Peer Review

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness

and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of general practitioners (GPs) and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to at least two lay reviewers in order to obtain comments from the patient's perspective.

It should be noted that all reviewers are invited to comment as individuals, not as representatives of any particular organisation or group. Corporate interests, whether commercial, professional, or societal have an opportunity to make representations at the national meeting stage where they can send representatives to the meeting or provide comment on the draft produced for that meeting. Peer reviewers are asked to complete a declaration of interests form.

The comments received from peer reviewers and others are carefully tabulated and discussed with the Chair and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

As a final quality control check prior to publication, the guideline and the summary of peer reviewers' comments are reviewed by the SIGN Editorial Group for that guideline to ensure that each point has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. Each member of the guideline development group is then asked formally to approve the final guideline for publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of antithrombotic therapy to treat and prevent thrombosis, maximize benefits and decrease risks

Potential Harms

Adverse effects associated with antithrombotic medications

Contraindications

Contraindications

- Contraindications to aspirin include: known allergy to the drug; use other than as an antiplatelet in children and adolescents under 16 years (risk of Reye's syndrome); active peptic ulceration; history of recent gastrointestinal bleeding; history of recent intracranial bleeding; and bleeding disorders including haemophilia, von Willebrand's disease, severe thrombocytopenia (e.g. platelets $<30x10^9$/l) and severe liver disease with coagulopathy.
- Contraindications to clopidogrel include active bleeding.
- Warfarin is contraindicated in patients with haemorrhagic stroke or significant bleeding.

Qualifying Statements

Qualifying Statements

Qualifying Statements

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is, however, advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (product licence). This is known as "off label" use. It is not unusual for medicines to be prescribed outwith their product licence and this can be necessary for a variety of reasons.
  Generally the unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.

  Medicines may be prescribed outwith their product licence in the following circumstances:

  - For an indication not specified within the marketing authorization
  - For administration via a different route
  - For administration of a different dose

  Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

  Any practitioner following a Scottish Intercollegiate Guidelines Network (SIGN) recommendation and prescribing a licensed medicine outwith the product licence needs to be aware that they are responsible for this decision, and in the event of adverse outcomes, may be required to justify the actions that they have taken.

  Prior to prescribing, the licensing status of a medication should be checked in the current version of the British National Formulary (BNF). The summary of product characteristics should also be consulted in the electronic medicines compendium (www.medicines.org.uk).

Implementation of the Guideline

Description of Implementation Strategy

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Refer to section 18 of the original guideline for information on resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1999 Mar (revised Aug 2012; republished 2013 Jun)

Guideline Developer(s)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

Source(s) of Funding

Scottish Executive Health Department

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group: Professor Mike Greaves, Professor of Haematology, University of Aberdeen *(Chair)*; Mr David Allan, Orthopaedic Surgeon, Southern General Hospital, Glasgow; Dr Janet Brennand, Consultant in Fetal and Maternal Medicine, Southern General Hospital, Glasgow; Dr Andrew Docherty, Consultant Cardiologist, Wishaw General Hospital; Mr Carl Fenelon, Clinical Pharmacist, Glasgow

Royal Infirmary; Dr Gregor Imrie, Consultant Anaesthetist, Southern General Hospital, Glasgow; Dr Martin Johnson, Consultant Respiratory Physician, Gartnavel General Hospital, Glasgow; Ms Joan Lawson, Lay Representative, Wick; Dr Chris Lush, Consultant Haematologist, Raigmore Hospital, Inverness; Dr Brian McInnes, Consultant Physician, Hairmyres Hospital, East Kilbride; Mr Gordon McPherson, Lay Representative, Langbank, Renfrewshire; Dr Andrew Moore, General Practitioner, Tain Health Centre; Dr Moray Nairn, Programme Manager, SIGN; Mrs Lindsay Robertson, Thrombosis Nurse, Glasgow Royal Infirmary; Mrs Lynne Smith, Information Officer, SIGN; Dr Ian Zealley, Consultant Radiologist, Ninewells Hospital, Dundee

Financial Disclosures/Conflicts of Interest

Declarations of interests were made by all members of the guideline development group. Further details are available from the Scottish Intercollegiate Guidelines Network (SIGN) Executive.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Antithrombotic therapy. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 1999. 70 p. (SIGN publication; no. 36). [186 references]

Any updates to the guideline that result from the availability of new evidence will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

This guideline was republished in June 2013.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Availability of Companion Documents

The following are available:

- Quick reference guide: Antithrombotic therapy. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2012 Aug. 18 p. Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .
- SIGN 50: A guideline developer's handbook. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2001 Feb. (SIGN publication; no. 50). Electronic copies available from the SIGN Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on January 3, 2002. The information was verified by the guideline developer as of February 4, 2002. This NGC summary was updated by ECRI Institute on October 2, 2012. This summary was updated by ECRI Institute on January 23, 2013 following the U.S. Food and Drug Administration advisory on Pradaxa (dabigatran etexilate mesylate). The information was republished by the guideline developer in June 2013 and updated by ECRI Institute on August 7, 2013. This summary was updated by ECRI Institute on March 10, 2014 following the U.S. Food and Drug Administration advisory on Low Molecular Weight Heparins.

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